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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/697,863	10/30/2003	David E. Clapham	110313.135US3	1595

23483 7590 10/30/2007

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EXAMINER	
WEGERT, SANDRA L	
ART UNIT	**PAPER NUMBER**
1647	

NOTIFICATION DATE	DELIVERY MODE
10/30/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/697,863	CLAPHAM ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-74* is/are pending in the application.

4a) Of the above claim(s) *2,7 and 26-74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6 and 8-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/4/05,5/13/05,5/17/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

Applicants' response and amendments submitted 15 November 2006 are acknowledged. In addition, the Information Disclosure Statements, sent 4 February 2005, 13 March 2005, and 17 March 2006 have been entered into the record.

Claims 75-111 have been cancelled. Claims 1-74 are pending in the instant application. Applicants' elections of Group I, drawn to CatSper1 nucleic acids in the reply filed on 15 November 2006 and SEQ ID NO: 1 in the reply filed 16 August 2007, are acknowledged. The elections were made without traverse. Claims 2, 7 and 26-74 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to non-elected Inventions, there being no allowable generic or linking claim.

Claims 1, 3-6 and 8-25, as reading on SEQ ID NO: 1, are under examination in the instant Office Action.

Claim Objections/Rejections

Claim Objections-

Claims 4, 8, 10 and 11 are objected to for reciting non-elected inventions (SEQ ID NO: 3 and 4).

Claim Rejections - 35 USC § 101 and 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 1, 3-6 and 8-25 are rejected under 35 U.S.C. 101 because the claimed invention lacks a specific and substantial asserted utility or a well-established utility.

The claims are directed to the nucleic acid of SEQ ID NO: 1 encoding the polypeptide of SEQ ID NO: 2, as well as large fragments of SEQ ID NO: 1. Further limiting claims are presented to a nucleic acid encoding a *CatSper1* protein, sequences with at least 80% identity to SEQ ID NO: 1, nucleic acids that hybridize to SEQ ID NO: 1, kits for detecting SEQ ID NO: 1, and vectors and host cells comprising SEQ ID NO: 1. However, the specification does not disclose a function for SEQ ID NO: 1, or the encoded polypeptide of SEQ ID NO: 2, in the context of the cell or organism.

No well-established utility exists for newly isolated complex biological molecules. However, the specification asserts the following as specific and substantial patentable utilities for the claimed polynucleotide and the polypeptide encoded by the claimed polynucleotide:

1) To make hybridization probes to detect the polynucleotide of SEQ ID NO: 1.

2) To produce the CATSPER polypeptide and fragments.

3) For use in the construction of "knock-in" or "knock-out" organisms.

4) For making antisense oligonucleotides.

5) In assays to screen for compounds capable of modifying the interaction between receptor and ligand.

6) In tissue typing.

7) As a Calcium channel.

Each of these shall be addressed in turn:

1) To make hybridization probes to detect the polynucleotide of SEQ ID NO: 1.

This asserted utility is not specific or substantial. Hybridization probes and primers can be designed from any polynucleotide sequence. The specification does not disclose specific cDNA, DNA, or RNA targets. Further, since this asserted utility is not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

2) To produce the CATSPER polypeptide and fragments. This asserted utility is also substantial, but not specific. Many nucleotide sequences can be used to make polypeptides. However, if the specification discloses nothing specific and substantial about the polynucleotides or polypeptides, both the polynucleotides and polypeptides produced have no patentable utility.

3) For use in the construction of "knock-in" or "knock-out" organisms. This asserted utility is not specific or substantial. The specification does not disclose diseases associated with a mutated, deleted, or translocated human CATSPER gene. Significant further experimentation would be required of the skilled artisan to identify any such a disease. The specification discloses nothing about the phenotypic result when the CATSPER gene is "knocked in" or "knocked out" or what specific tissues and cells are being targeted. Since this asserted utility is

not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

4) For making antisense oligonucleotides. This asserted utility is not specific or substantial. Such can be performed for any polynucleotide. Further, the specification does not disclose diseases or conditions associated with the human CATSPER gene. Significant further experimentation would be required of the skilled artisan to identify individuals in need of antisense treatment, to determine the route of administration of the antisense, as well as to determine gene targets and quantity and duration of treatment. Since this asserted utility is also not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

5) In assays to screen for compounds capable of modifying the interaction between receptor and ligand. This asserted utility is substantial but not specific. Such can be performed for any receptor transfected into a cell and any receptor-ligand pair. Additionally, the specification discloses nothing specific or substantial for the compounds that can be identified by this method.

6) *In tissue typing.* This asserted utility is not substantial or specific. Such assays can be performed with any polynucleotide; thus, the asserted utility is not specific. Furthermore, the specification discloses limited tests of tissue expression. For example, the channel expressed by SEQ ID NO: 3 was tested for tissue expression, but that produced by the nucleic acid of SEQ ID NO: 1 (the claimed nucleic acid) was not. Applicant implies that the expression pattern for SEQ ID NO: 3 supports a useful function of the polynucleotide of SEQ ID NO: 1. However, there is no demonstrated connection between the polynucleotide of SEQ ID NO: 1 and that of SEQ ID

NO: 3. Furthermore, patentable utility of tissue typing for the claimed polynucleotide encoding the CATSPER polypeptide is not substantial even if tissue expression had been tested for the claimed polynucleotide, because one skilled in the art would not readily use the nucleotide sequences for tissue-typing in a real world sense as the protein is not specific to one tissue and is not associated with any disease or disorder. This asserted utility is also not specific because numerous unrelated nucleotide sequences would also show a similar tissue-typing pattern. In addition, evidence of mere expression in a tissue is not tantamount to a showing of a role for the polynucleotide of the present invention. It is not clear if the polynucleotide of the present invention is correlated with a specific change in physiology, for example, or with a disease state. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

7) *As a Calcium channel.* This asserted utility is credible and specific, but not substantial. The specification discloses that the polypeptide encoded by SEQ ID NO: **3** (mouse CATSPER) is a sperm-specific calcium channel necessary for sperm motility (see Specification, p. 57). Such data have *not* been collected for the claimed nucleic acid of SEQ ID NO: 1 or the polypeptide encoded by SEQ ID NO: 1. In fact with its low homology to the CATSPER family of proteins (31% homology at best), it cannot be determined if the claimed nucleic acid actually is a CATSPER channel or even a calcium channel. Furthermore, members of the large family of Calcium channel proteins share several recognizable structural similarities, yet have diverse functions (see, for example: N.A., Suppl 1, Trends Pharmacol. Sci., 1997, 18: 77-84; Lehmann-Horn et al., 1999, Physiol Rev 79(4): 1317-1372, Table 2). The specification does not disclose characteristics specific to a voltage-gated channel (e.g., Nernst potential, conductance, reversal

potential, ion selectivity, etc), any blockers, its physiological role in the organism, or a link between the channel and a specific condition or disease state. Determination of any of these would require significant further research. Since the asserted utility is not available as a real world use, and significant further research beyond the disclosure is required, the asserted utility is not substantial.

Claims 1, 3-6 and 8-25 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The specification does not teach the skilled artisan how to use the claimed polynucleotides encoding the polypeptide of SEQ ID NO: 2 for any specific and substantial purpose. For example, there is no disclosure of particular disease states correlating to an alteration in levels or forms of the polypeptide such that the polynucleotide could be used as a diagnostic tool. The skilled artisan is not provided with sufficient guidance to use the claimed polynucleotides for any purpose.

There are many factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of

experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (FED. Cir. 1988). In the instant case, the only evidence of function given for SEQ ID NO: 1 is the sequence itself. There is no example or reduction to practice to show that SEQ ID NO: 1 has a substantial organismal function, or that it can even be associated with the genus of CATSPER channels that does have a substantial function.

Due to the large quantity of experimentation necessary to determine an activity or property of the claimed polynucleotide and disclosed polypeptides such that it can be determined how to use the claimed polynucleotide of SEQ ID NO: 1 and to screen for activity, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which fail to recite particular biological activities- undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Furthermore, applicants are not enabled for *fragments* or *variants* of polynucleotides: 1) at least 10-18 consecutive bases long, 2) identified by substructures of the encoded protein (such as the transmembrane domain), 3) having at least 80% sequence identity, or 4) that hybridize to the claimed nucleic acid at low or moderate stringency, as recited in Claims 1, 3-6, 8, 10 and 11, and embraced by claims 1, 3-6 and 8-25. Furthermore, even if there were a patentable use for the claimed full-length polynucleotide (SEQ ID NO: 1), the claimed variants would not be enabled because the specification has not taught one of ordinary skill in the art how to use them or fragments thereof. For these reasons, it is not predictable as to which nucleic acids are necessary to maintain the functional characteristics of the claimed polynucleotide.

35 USC § 112, first paragraph - Written Description.

Claims 1, 3-6, 8, 10 and 11 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The claims are directed to nucleotide(s) which encode the polypeptide of SEQ ID NO: 2. Further claim limitations are presented to nucleic acids at least 10-18 consecutive bases long, encoding at least the transmembrane domain (as well as other domains), having at least 80% sequence identity, and those that hybridize to the claimed nucleic acid under hybridization conditions that include a wash step of 1.0X SSC at 65° C.

The specification teaches a polynucleotide (SEQ ID NO: 1) and a polypeptide (SEQ ID NO: 2). However, the specification does not teach functional or structural characteristics of all claimed polynucleotides. The description of one polynucleotide encoding a presumed CATSPER polypeptide (SEQ ID NO: 2) is not adequate written description of an entire genus of functionally equivalent polynucleotides and polypeptides.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product,

or any combination thereof. In this case, the only factor present in the claims is a partial structure in the form of a recitation of percent identity or domains that have not been adequately identified. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

With the exception of the full-length sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of all claimed polynucleotides, and therefore, would not know how to use them. Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of making. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of use. The nucleotide *itself* is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine

sequence.

Therefore, only an isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1 and a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections- 35 USC § 102

The following are quotations of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 8, 10, and 12 are rejected under 35 U.S.C. 102(b) as being unpatentable over Sanger Centre (1998, Science, 282: 2012-2018, Accession No. Z82256.1). The Sanger Centre Consortium discloses a polynucleotide sequence encoding a nematode sodium channel which is 29% identical to SEQ ID NO: 1 in the instant application. There are several short identical areas where the nucleotides are the same, such as in the region of residues 174-181. This reference meets the limitations of claims 8, 10, and 12 which cite "at least *a portion* of SEQ ID NO: 1," as well as hybridization steps that are not stringent (i.e., washing at 65°C).

Conclusion: Claims 1, 3-6 and 8-25 are rejected for the reasons recited above.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Manjunath Rao, can be reached at (571) 272-0939.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

SLW
20 October 2007

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646